

Appendix A

Claim Amendments

1. (Currently amended) ~~Method A~~ method for preparing a sterile aqueous suspension of ciclesonide suitable for nebulization comprising the steps of:
  - a. providing an aqueous suspension of ciclesonide, containing one or more pharmaceutically acceptable excipients, which one or more excipients are all non-ionic excipients; and
  - b. autoclaving the aqueous suspension provided in (a).
  
2. (Currently amended) ~~Method A~~ method for preparing a sterile aqueous suspension of ciclesonide suitable for nebulization comprising the steps of:
  - a. providing an aqueous suspension of ciclesonide, containing at least one non-ionic agent for adjusting ~~the~~ osmolality and optionally further pharmaceutically acceptable excipients; and
  - b. autoclaving the aqueous suspension provided in (a).

3. (Currently amended) ~~Method~~ The method according to claim 1 ~~[[or 2]]~~, wherein ciclesonide is selected from the group consisting of  $[11\beta, 16\alpha(R)]$ -  
-16,17-[(cyclohexylmethylene)bis(oxy)]-  
11-hydroxy-21-(2-methyl-1-oxopropoxy)pregna-1,4diene-  
3,20-dione, mixtures of the compounds  ~~$[11\beta, 16\alpha(S)]$ -~~  
~~16,17-[(cyclohexylmethylene)bis(oxy)]-11-hydroxy-21-~~  
~~(2-methyl-1-oxopropoxy)pregna-1,4-diene-3,20-dione)~~  $[11\beta$   
,16 $\alpha$ (S)]-16,17-[(cyclohexylmethylene)bis-  
(oxy)]-11-hydroxy-21-(2-methyl-1-oxopropoxy)pregna-  
1,4-diene-3,20-dione) and  $[11\beta, 16\alpha(R)]$ -  
-16,17-[(cyclohexylmethylene)bis(oxy)]-  
11-hydroxy-21-(2-methyl-1-oxopropoxy)pregna-1,4-diene-  
3,20-dione in any desired mixing ratio, and mixtures of  
the compounds  ~~$[11\beta, 16\alpha(S)]$ -16,17-[(cyclohexylmethy-~~  
~~lene)bis(oxy)]-11-hydroxy-21-~~  
~~(2-methyl-1-oxo-~~  
~~propoxy)pregna-1,4-diene-3,20-dione)~~  $[11\beta, 16\alpha(S)]$ -  
16,17-[(cyclohexylmethylene)bis-  
(oxy)]-11-hydroxy-21-(2-methyl-1-oxopropoxy)pregna-  
1,4-diene-3,20-dione) and  ~~$[11\beta, 16\alpha(R)]$ -~~  
~~16,17-[(cyclohexylmethylene)bis(oxy)]-~~  
~~11-hydroxy-~~  
~~21-(2-methyl-1-oxopropoxy)pregna-1,4-diene-3,20-dione~~

which ~~essentially consist~~ [11 $\beta$ ,16 $\alpha$ (R)]-  
-16,17-[(cyclohexylmethylene)bis(oxy)]-11-hydroxy-  
-21-(2-methyl-1-oxopropoxy)pregna-1,4-diene-3,20-dione  
consisting essentially of R epimers.

4. (Currently amended) ~~Method~~ The method according to claim 1 ~~[[or 2]]~~, wherein ciclesonide is selected from the group consisting of ciclesonide, solvates of ciclesonide, physiologically functional derivatives of ciclesonide, solvates of physiologically functional ~~derivates~~ derivatives of ciclesonide and mixtures thereof.

5. (Currently amended) ~~Method~~ The method according to claim 4, wherein the physiologically functional derivative of ciclesonide is selected from the group consisting of 16 $\alpha$ ,17-(22R)-cyclohexylmethylenedioxy-11 $\beta$ ,21-dihydroxypregna-1,4-diene-3,20-dione, 16 $\alpha$ ,17-(22S)-cyclohexylmethylenedioxy-11 $\beta$ ,21-dihydroxypregna-1,4-diene-3,20-dione, and mixtures thereof in any mixing ratio.

6. (Currently amended) ~~Method~~ The method according to claim 1 ~~[[or 2]]~~, wherein the mean particle size of ciclesonide is less than 12 $\mu$ m, ~~preferably from 1 to 7 $\mu$ m, preferably 2 to 6 $\mu$ m, particularly preferably 2 to 4 $\mu$ m.~~
  
7. (Currently amended) ~~Method~~ The method according to claim 2, wherein the non-ionic agent for adjusting the osmolality is selected from the group consisting of mannitol, glycerol, glucose, lactose, trehalose, sucrose, propylene glycol, sorbitol, xylitol, polyethylene glycol, ethanol, isopropanol, cyclodextrins, derivatives of ~~cyclodextrines~~ cyclodextrins and mixtures thereof.
  
8. (Currently amended) ~~Method~~ The method according to claim 7, wherein the agent for adjusting the osmolality is selected from the group consisting of mannitol, glycerol, glucose and mixtures thereof.
  
9. (Currently amended) ~~Method~~ The method according to claim 1, wherein the suitable excipients are selected from the group consisting of agents for adjusting osmolality, suspending agents, agents for modifying

[[the]] pH of the suspension, chelating agents, preservatives and mixtures thereof.

10. (Currently amended) ~~Method~~ The method according to claim 2, wherein the suitable excipients are selected from the group consisting of suspending agents, agents for modifying [[the]] pH of the suspension, chelating agents, preservatives and mixtures thereof.

11. (Currently amended) ~~Method~~ The method according to claim 10, wherein suitable excipients are non-ionic excipients.

12. (Currently amended) ~~Method~~ The method according to claim 9 [[or 10]], wherein an agent for modifying the pH of the suspension is present as excipients; which is an organic acid selected from the group consisting of citric acid, tartaric acid, lactic acid and mixtures thereof.

13. (Currently amended) ~~Method~~ The method according to claim 9 [[or 10]], wherein the suspending agent is selected from the group consisting of polysorbates, tyloxapol, poloxamers, poloxamines, polyoxyethylene

castor oil derivatives, phospholipids,  
hydroxypropylmethylcellulose, hydroxypropylcellulose,  
hydroxyethylcellulose, methylcellulose,  
polyvinylpyrrolidone, polyvinylalcohol and mixtures  
thereof.

14. (Currently amended) ~~Method~~ The method according to  
claim 13, wherein the suspending agents are  
polyoxyethylene sorbitan fatty acid esters ~~(polyserbate)~~.

15. (Currently amended) ~~Method~~ The method according to  
claim 1, comprising the steps of  
a. dissolving the non-ionic excipients or excipients  
in water;  
b. optionally filtering the solution;  
c. homogeneously suspending ciclesonide within the  
solution and  
d. autoclaving the aqueous suspension provided in  
(c).

16. (Currently amended) ~~Method~~ The method according to  
claim 2, comprising the steps of

- a. dissolving the non-ionic agent for adjusting the osmolality and optionally other excipients in water;
- b. optionally filtering the solution;
- c. homogeneously suspending ciclesonide within the solution; and
- d. autoclaving the aqueous suspension provided in (c).

17. (Currently amended) ~~Method~~ The method according to claim 1 ~~any of the preceding claims~~, wherein autoclaving is carried out at a temperature above 90°C.

18. (Currently amended) ~~Method~~ The method according to claim 17, wherein autoclaving is carried out at a temperature above 120° C.

19. (Currently amended) ~~Method~~ The method according to claim 17, wherein autoclaving is carried out at 121°C for at least 15 minutes.

20. (Currently amended) ~~Method~~ The method according to claim 1 ~~[[or 2]]~~, wherein the sterile aqueous suspension

of ciclesonide suitable for nebulization has an osmolality in the range of 225- 430 mosmol/kg, ~~in the range of 250 to 350 mosmol/kg or in the range of 280 to 300 mosmol/kg.~~

21. (Currently amended) ~~Sterile~~ A sterile aqueous suspension of ciclesonide suitable for nebulization containing one or more pharmaceutically acceptable excipients, which one or more excipients are all non-ionic excipients.

22. (Currently amended) ~~Sterile~~ A sterile aqueous suspension of ciclesonide suitable for nebulization containing at least one non-ionic agent for adjusting ~~[[the]]~~ osmolality and optionally further pharmaceutically acceptable excipients.

23. (Currently amended) ~~Sterile~~ The sterile aqueous suspension according to claim 21 ~~claims 21 or 22~~, having an osmolality in the range of 225- 430 mosmol/kg, ~~in the range of 250 to 350 mosmol/kg or in the range of 280 to 300 mosmol/kg.~~



24. (Currently amended) ~~Sterile~~ The sterile aqueous suspension according to claim 21 ~~elaims 21 or 22~~, wherein the ~~mean particle size of~~ ciclesonide has a mean particle size of ~~[[is]]~~ less than 12 $\mu$ m, ~~preferably from 0.1 to 8 $\mu$ m, preferably 1 to 6 $\mu$ m, particularly preferably 2 to 4 $\mu$ m.~~

25. (Currently amended) ~~Sterile~~ The sterile aqueous suspension according to claim 22, wherein the non-ionic agent for adjusting the osmolality is selected from the group consisting of mannitol, glycerol, glucose, lactose, trehalose, sucrose, propylene glycol, sorbitol, xylitol, polyethylene glycol, ethanol, isopropanol, cyclodextrins, derivatives of cyclodextrins ~~cyclodextrines~~ and mixtures thereof.

26. (Currently amended) ~~Sterile~~ The sterile aqueous suspension according to claim 25, wherein the agent for adjusting the osmolality is selected from the group consisting of mannitol, glycerol, glucose and mixtures thereof.

27. (Currently amended) ~~Sterile~~ The sterile aqueous suspension according to claim 21, wherein the suitable excipients are selected from the group consisting of agents for adjusting osmolality, suspending agents, agents for modifying ~~[[the]]~~ pH of the suspension, chelating agents, preservatives and mixtures thereof.

28. (Currently amended) ~~Sterile~~ The sterile aqueous suspension according to claim 22, wherein the suitable excipients are selected from the group consisting of suspending agents, agents for modifying ~~[[the]]~~ pH of the suspension, chelating agents, preservatives and mixtures thereof. ~~[[.]]~~

29. (Currently amended) ~~Sterile~~ The sterile aqueous suspension according to claim 22, wherein suitable excipients are non-ionic excipients.

30. (Currently amended) ~~Sterile~~ The sterile aqueous suspension according to claim 27 ~~[[or 28]]~~, wherein an agent ~~agents~~ for modifying the pH of the suspension is present as an excipient ~~excipients~~ which is an organic

acid selected from the group consisting of citric acid, tartaric acid, lactic acid and mixtures thereof.

31. (Currently amended) ~~Sterile~~ The sterile aqueous suspension according to claim 27 ~~[[or 28]]~~, wherein the suspending agent is selected from the group consisting of polysorbates, tyloxapol, poloxamers, poloxamines, polyoxyethylene castor oil derivatives, phospholipids, hydroxypropylmethylcellulose, hydroxypropylcellulose, hydroxyethylcellulose, methylcellulose, polyvinylpyrrolidone, polyvinylalcohol and mixtures thereof.

32. (Currently amended) ~~Sterile~~ The sterile aqueous suspension according to claim 31, wherein the suspending agents ~~polyorbate~~ are polyoxyethylene sorbitan fatty acid esters ~~(polyorbate)~~.

33. (Currently amended) ~~Aqueous~~ An aqueous suspension of ciclesonide for administration by nebulization, wherein the concentration of ciclesonide within the suspension for nebulization is in the range of 0.005% to 0.5% (w/v) ~~(i.e. 0.05 mg/ml to 5mg/ml)~~.

34. (Currently amended) ~~Aqueous~~ The aqueous suspension according to claim 21, ~~22 or 33,~~ wherein the ~~mean particle size of~~ ciclesonide has a mean particle size of ~~[[is]] less than 12µm, preferably from 0.1 to 8µm, preferably 1 to 6µm, particularly preferably 2 to 4µm.~~

35. (Currently amended) ~~Aqueous~~ The aqueous suspension of ciclesonide according to claim 33, which is a sterile suspension.

36. (Currently amended) The sterile aqueous suspension according to claim 21 for administration by nebulization, wherein the concentration of ciclesonide within the suspension for nebulization is in the range of 0.005% to 0.5% (w/v) ~~Aqueous suspension of ciclesonide according to claim 33, which is a formulation according to claim 21 or 22.~~

37. (Currently amended) ~~Sterile~~ The sterile aqueous suspension ~~suspensions~~ according to claim 21 ~~[[or 22]]~~ containing as excipients mannitol and polysorbate or glycerol and polysorbate.

38. (Currently amended) ~~Sterile~~ The sterile aqueous suspension according to claim 37, additionally containing hydrochloric acid or citric acid.

39. (Currently amended) ~~Method~~ A method for the prophylaxis or treatment of a clinical condition in a patient for which a glucocorticosteroid is indicated, which comprises administration of a therapeutically effective amount of a sterile aqueous suspension of ciclesonide according to claim 21, ~~22 or 33~~.

40. (Currently amended) ~~Method~~ The method according to claim 39, wherein the clinical condition is asthma the patient is a child and the treatment is a continuous treatment regimen and the sterile aqueous suspension of ciclesonide is administered by nebulization.

41. (Currently amended) ~~Drug~~ A drug product comprising a sealed container containing a sterile aqueous suspension according to claim 21, ~~22 or 33~~, and a label indicating administration by nebulization in a continuous treatment regimen.